

Original Research

The Interaction Between Dietary Fructose and Magnesium Adversely Affects Macromineral Homeostasis in Men

David B. Milne, PhD, and Forrest H. Nielsen, PhD

United States Department of Agriculture, Agricultural Research Service, Grand Forks Human Nutrition Research Center, Grand Forks, North Dakota 58202

Key words: magnesium balance, calcium metabolism, calcium balance, phosphorous balance

Objective: Studies with rats have found that an interaction between fructose and magnesium affects macromineral metabolism; high dietary fructose significantly increased kidney calcification in both male and female rats, particularly when dietary magnesium was low. This study tests the hypothesis that an interaction between dietary fructose and magnesium adversely affects macromineral homeostasis in men.

Methods: Eleven men aged 22 to 40 years were fed a mixed, Western diet for four 42-day dietary periods in which dietary magnesium was either approximately 170 or 370 mg/day and dietary fructose was either 4% or 20% of energy. A decaffeinated beverage containing high fructose corn syrup replaced cornstarch, bread and rice in the low fructose diet to give the high fructose diet.

Results: High dietary fructose significantly ($p < 0.01$) increased magnesium balance during both low and high dietary magnesium intakes. Ultrafilterable and ionized serum magnesium also apparently were related to magnesium and fructose intakes; they were higher when fructose was fed and when Mg intakes were high. High fructose depressed calcium balance: the effect tended to be more marked when dietary Mg was low. High dietary fructose also significantly ($p < 0.005$) decreased phosphorous balance. Urinary phosphorous losses were significantly ($p < 0.001$) higher when high dietary fructose was fed. High dietary fructose also increased the concentration of serum alkaline phosphatase ($p < 0.005$).

Conclusion: These findings indicate that dietary fructose adversely affects macromineral homeostasis in humans and suggest further studies to see if a high fructose diet coupled with low dietary magnesium and marginal calcium leads to bone loss.

INTRODUCTION

Refined sugar use has declined over the last 20 years, whereas high-fructose corn sweetener consumption has increased by more than 700% [1]. The ingestion of fructose at about 20% of dietary energy has been implicated in the induction of detrimental changes in indices associated with ischemic heart disease, gout and urolithiasis, when compared with starch. At least two studies [2,3] with both men and women demonstrated increases in total triglycerides, total cholesterol, LDL cholesterol and uric acid when high amounts of fructose were

fed. Fructose also increased fasting serum glucose and increased urinary oxalate excretion.

Studies with animals have also demonstrated that dietary fructose at 20% of energy, when compared with starch, exacerbated signs of both copper and magnesium deficiencies [4,5]. Several studies document the induction of nephrocalcinosis in rats fed diets deficient in magnesium and high in sucrose [6,7]. Recently, a synergistic interaction between high dietary fructose and magnesium deficiency on kidney calcification was found [5]. Koh and Min [8] compared the interaction in male and female rats. High dietary fructose significantly increased

Address reprint requests to: Forrest H. Nielsen, PhD, USDA/ARS, GFHNRC, PO Box 9034, Grand Forks, ND 58202-9034.

The U.S. Department of Agriculture, Agricultural Research Service, Northern Plains Area, is an equal opportunity/affirmative action employer and all agency services are available without discrimination. Mention of a trademark or proprietary product does not constitute a guarantee or warranty of the product by the United States Department of Agriculture and does not imply its approval to the exclusion of other products that may also be suitable.

kidney calcium in female rats fed deficient or adequate magnesium diets and in male rats fed the magnesium deficient diet only. The greatest kidney calcification occurred in female rats fed the high fructose and magnesium deficient diet. Fructose feeding also increased plasma calcium and magnesium.

Dietary surveys made since 1965 [9,10] indicate that self-selected diets provide marginal or suboptimal magnesium intakes, based on the recommended dietary allowances (RDA), for a significant percentage of adults. Because high dietary fructose consumption concomitant with magnesium intakes less than the recommended dietary allowance is likely a common occurrence, particularly in individuals consuming large amounts of soft drinks and eating few green vegetables, and because fructose and magnesium act synergistically to affect variables they independently adversely affect in rats, we designed the following study to test the hypothesis that an interaction between dietary fructose and magnesium adversely affects macromineral homeostasis in men.

METHODS

Healthy men aged 22 to 40 years were admitted to the study after they had been informed in detail of the nature of the research and associated risks and after medical, psychological and nutritional evaluations had established that they had no underlying disease and that they were emotionally suited for the project. Protocols were approved by the Institutional Review Boards of the University of North Dakota and the United States Department of Agriculture and followed the guidelines

of the Department of Health and Human Services and the Helsinki doctrine regarding the use of human subjects.

The men were maintained in a metabolic unit under close supervision for approximately six months and fed a constant, weighed diet (Tables 1a and 1b), on a three-day menu rotation, that was low in magnesium (170 mg Mg/2500 kcal, by analysis). The diet was adequate in all other nutrients. After a 16-day equilibration period with starch at 20% of energy in a diet supplemented with 205 mg of magnesium per day, the study was divided into four 42-day dietary periods in a randomized, double-blind, 2×2 factorial design. Magnesium was varied at 170 and 370 mg/2500 kcal and starch and fructose at 20% of energy. Magnesium was supplemented as magnesium gluconate. Fructose was supplied mainly as high fructose corn sweetener in commercial sodas (Table 1a). The dietary intake of each subject was based on energy needs, as calculated by the Harris and Benedict equation [11], plus an additional 50% of basal energy expenditure for normal activity. During the study, energy intakes were adjusted to maintain the body weight to within $\pm 2\%$ of admission weight by adjusting the amount of the basal diet in 200 kcal increments.

All food was weighed during preparation in the metabolic kitchen, and it was eaten quantitatively by the subjects. Urine and feces were collected carefully to avoid trace mineral contamination. Duplicate diets at the 2500 kcal level were prepared daily for analysis and blended in a plastic blender with stainless steel blades. Adjustments for differences in energy intakes were calculated proportionately.

Magnesium, calcium and phosphorus were determined in aliquots of six-day composites of diets and feces. They were

Table 1a. Fructose Diet Used in High Dietary Fructose & Mg Deprivation in Men's Study

Fructose Diet		
Day 1	Day 2	Day 3
Cola, decaffeinated	Cola, decaffeinated	Cola, decaffeinated
Canadian Bacon & Cheese Muffin	Ham & Cheese Muffin	Hot Wheat Cereal
Baked Eggs w Hash Browns	Baked Eggs	Baked Eggs
Blueberries	Mandarin Oranges	White Bread
Half & Half Cream		Margarine
		Diet Strawberry Preserves
Cola, decaffeinated	Cola, decaffeinated	Cola, decaffeinated
Ham & Broccoli Casserole	Pepperoni Pizza	Cottage Pasta Bake
2% Cottage Cheese	Lettuce Salad	Tossed Salad
Baked Apples	French Dressing	Ranch Dressing
	Sugar Cookie	Sugar Cookie
Cola, decaffeinated	Cola, decaffeinated	Cola, decaffeinated
Chicken Rice Casserole	Beef Stew	Crispy Chicken
Lettuce Salad	2% Cottage Cheese	Rice Pilaf
Ranch Dressing	Baked Peaches	Baked Green Beans
Sugar Cookie		
Cola, decaffeinated	Cola, decaffeinated	Cola, decaffeinated
Soda Crackers	Vanilla Wafers	Cheesecake
Cream Cheese	Diet Cherry Gelatin	Peaches

Table 1b. Starch Diet Used in High Dietary Fructose & Mg Deprivation in Men's Study

Starch Diet		
Day 1	Day 2	Day 3
Cherry Drink Mix	Cherry Drink Mix	Cherry Drink Mix
Canadian Bacon & Cheese Muffin	Ham & Cheese Muffin	Hot Wheat Cereal
Baked Hash Browns	Mandarin Oranges	White Bread
Blueberries		Margarine
Half & Half Cream		Diet Strawberry Preserves
Cherry Drink Mix	Cherry Drink Mix	Cherry Drink Mix
Ham & Broccoli Casserole	Pepperoni Pizza	Cottage Pasta Bake
2% Cottage Cheese	Lettuce Salad	Tossed Salad
Apple Crisp	French Dressing	Ranch Dressing
	Sugar Cookie	White Dinner Roll
		Margarine
		Sugar Cookie
Cherry Drink Mix	Cherry Drink Mix	Cherry Drink Mix
Chicken Rice Casserole	Beef Stew	Crispy Chicken
Lettuce Salad	2% Cottage Cheese	Rice Pilaf
Ranch Dressing	White Dinner Roll	Baked Green Beans
White Dinner Roll	Margarine	White Dinner Roll
Margarine	Peach Crisp	Margarine
Sugar Cookie		
Soda Crackers	Vanilla Wafers	Cheesecake
Cream Cheese	Diet Cherry Gelatin	Peaches

measured by inductively coupled argon plasma emission spectroscopy (ICAP) (Thermal ARL-VG Elemental, Div. of Thermal Jarell Ash Corp., Franklin, MA 02038) [12] after wet digestion of aliquots of freeze-dried, blended material with nitric and perchloric acids [13]. Urinary magnesium, calcium and phosphorus were determined by ICAP analysis of a diluted aliquot. Concurrent replicate analysis of a Total Diet SRM #1548 (n=8) (National Institute of Standards and Technology, Gaithersburg, MD 20899) yielded values of 1675 ± 23 , 531 ± 4 , and 3240 ± 84 $\mu\text{g/g}$ as compared with certified values of

1740 ± 70 , 556 ± 27 , and 3240 ± 40 $\mu\text{g/g}$ for Ca, Mg and P, respectively. A fecal pool analyzed concurrently (n=14) yielded values of 40.1 ± 1.3 , 13.1 ± 0.5 , and 24.6 ± 1.3 mg/g as compared with expected ranges of 35.0 to 45.0, 10.1 to 13.2, and 23.0 to 28.0 mg/g for Ca, Mg, and P, respectively.

Blood was drawn into plastic syringes from an antecubital vein, which had been made visible by temporary use of a tourniquet, after the subjects had fasted for 10 hours. Aliquots were mixed with appropriate anticoagulants and processed within 90 minutes of the time the blood was drawn. Serum magnesium and calcium concentrations were determined by flame atomic absorption spectrophotometry after dilution 50-fold with an acidic lanthanum chloride diluent [14]. Ionized calcium and magnesium were determined by using a NOVA CRT 8+ electrolyte analyzer (Nova Biomedical, Waltham, NJ 02254). Serum ultrafiltrates were prepared by using an Amicon MPS-1 filter system (Amicon, Inc., Beverly, MA 01915) and a procedure described by D'Costa and Cheng [15]. The magnesium content of the ultrafiltrate was determined by ICAP analysis [12]. Serum phosphate was determined by a modification of an automated procedure described by Daly *et al.* [16]. Parathyroid hormone (PTH) and osteocalcin were determined by using commercially available radioimmunoassay kits (Instar, Stillwater, MN 55082).

Data were analyzed by repeated measures analysis of variance [17]. Differences with *p* values ≤ 0.05 were considered significant.

RESULTS

Magnesium balance was independently affected by both magnesium and fructose intakes in the eleven men who completed the study (Table 2). Magnesium balance and fecal and urinary magnesium were all directly related to magnesium intake. Substituting high fructose for starch resulted in higher magnesium balance at both low and high magnesium intake.

Table 2. Magnesium Balance

Treatment	(mg/day)			
	Diet Mg	Urine Mg	Fecal Mg	Mg Balance
Starch-low Mg	165	87	89	-12
Starch-high Mg	370	131	209	30
Fructose-low Mg	176	89	84	3
Fructose-high Mg	370	133	184	53
Analysis of Variance <i>p</i> Values				
Magnesium		0.0001	0.0001	0.0001
Fructose		0.59	0.02	0.01
Mg X Fructose		0.55	0.06	0.64
Pooled SD		10	17	23

Mean all 6-day balance periods.

Eleven subjects.

Table 3. Calcium Balance

Treatment	Diet Ca (mg/day)	Fecal Ca		Urine Ca		Ca Balance (mg/day)
		(mg/day)	(% intake)	(mg/day)	(% intake)	
Starch low Mg	1144	743	65.2	226	19.9	175
Starch high Mg	1155	769	67.4	245	21.6	142
Fructose low Mg	1011	711	71.1	223	22.3	77
Fructose high Mg	1014	676	67.2	225	22.7	113
Analysis of Variance <i>p</i> Values						
Magnesium		0.97	0.81	0.29	0.28	1.00
Fructose		0.008	0.07	0.08	0.01	0.007
Mg X Fructose		0.10	0.07	0.40	0.60	0.14
Pooled SD		66	6.0	20	2.2	79

Mean all 6-day balance periods.
Eleven subjects.

Table 4. Phosphorus Balance

Treatment	Diet P (mg/day)	Fecal P		Urine P		P Balance (mg/day)
		(mg/day)	(% intake)	(mg/day)	(% intake)	
Starch low Mg	1448	441	31.6	941	65.2	66
Starch high Mg	1454	448	31.2	943	65.1	64
Fructose low Mg	1528	404	26.9	1168	76.8	-44
Fructose high Mg	1509	402	27.2	1110	74.4	-4
Analysis of Variance <i>p</i> Values						
Magnesium		0.81	0.92	0.07	0.16	0.43
Fructose		0.06	0.02	0.0001	0.0001	0.005
Mg X Fructose		0.13	0.94	0.25	0.75	0.61
Pooled SD		65	5.2	60	4.5	99

Mean all 6-day balance periods.
Eleven subjects.

Table 5. Serum Indicators of Calcium and Magnesium Status¹

	Calcium (mg/dL)	Ionized Ca (mg/dL)	Magnesium (mg/dL)	Ionized Mg (mg/dL)	Ultrafilterable Mg (mg/dL)	Alkaline Phosphatase (U/L)
Starch low Mg	9.20	5.30	2.02	1.34	1.40	86
Starch high Mg	9.09	5.29	2.03	1.36	1.45	91
Fructose low Mg	9.13	5.28	2.06	1.36	1.45	98
Fructose high Mg	9.14	5.39	2.07	1.39	1.48	100
Analysis of Variance <i>p</i> Values						
Magnesium	0.51	0.71	0.66	0.07	0.02	0.65
Fructose	0.62	0.79	0.15	0.08	0.04	0.001
Fructose X Mg	0.41	0.45	0.94	0.81	0.57	0.81
Pooled SD	0.19	0.34	0.08	0.05	0.05	7

¹ Mean of last 10 days of each diet period.

Urinary excretion of magnesium was unaffected by elevated dietary fructose, but fecal excretion was decreased at both levels of magnesium intake. This indicated increased absorption and retention of magnesium during periods of higher fructose intake. The men were in negative magnesium balance when fed the starch diet containing 165 mg magnesium per day.

Conversely, both calcium and phosphorus balances were decreased significantly by the high fructose intake (Tables 3 and 4); the lowest for both occurred during the high fructose-low magnesium intake period. Fecal phosphorus was lower and

urinary phosphorus was elevated when fructose was fed. Even with slightly higher phosphorus intake when high fructose was fed, the men were in negative phosphorus balance; phosphorus balance was most negative during the low magnesium-high fructose diet period.

Total serum calcium and magnesium and ionized calcium were unaffected by the diets (Table 5). Ionized magnesium and ultrafilterable magnesium, indicators of the biologically important fraction, were affected by both magnesium and fructose intakes. They were directly related to magnesium intake and

slightly elevated by high dietary fructose. Serum alkaline phosphatase was significantly ($p < 0.001$) elevated when dietary fructose was high (Table 5), whereas serum phosphate, osteocalcin and parathyroid hormone were not affected by dietary treatment (data not shown).

DISCUSSION

The negative magnesium balance and the lowest concentrations of ionized and ultrafilterable magnesium found when the men were fed the low magnesium starch diet indicated that they were becoming magnesium depleted. This indicates that 165 mg magnesium per day is not adequate and is consistent with estimates of magnesium requirements of 4 to 5 mg magnesium per kg body weight per day or 280 to 350 mg per day for a 70 kg man [18]. It is likely that if sweat and integumentary losses were included, the men would have been in negative magnesium balance when high dietary fructose and 175 mg magnesium per day were fed.

The findings from this study support the hypothesis that high dietary fructose affects macromineral homeostasis in humans. The increase in magnesium balance when fructose was fed is consistent with observations by Holbrook *et al.* [19], who found increased absorption and retention of magnesium and other minerals when fructose was fed as compared with starch. However, in the same study the authors also reported a more positive balance for calcium when fructose was fed as opposed to starch, contrary to what was seen in this study. A likely difference could be that in the study of Holbrook *et al.* [19], calcium intakes were much lower when starch was fed and higher when high dietary fructose was fed. Our results for calcium were more consistent with those of Hallfrisch *et al.* [20], who found decreased calcium balance when simple sugars were fed compared with complex carbohydrates, and Ivaturi and Kies [21] who reported lower calcium balance when fructose was fed than when sucrose was fed.

The mechanisms by which fructose affects magnesium absorption and balance are largely unknown. It has been hypothesized that fructose may form complexes with mineral elements, such as magnesium, in the gut and these complexes may facilitate mineral absorption. Fructose is readily absorbed by man and rats without conversion to other sugars via facilitated diffusion [22]. Thus a magnesium-fructose complex may be more readily absorbed. This hypothesis is consistent with observations of Van Der Heijden *et al.* [23], who suggested that fructose enhanced the ileal solubility of magnesium, which in turn elevates the amount of magnesium that can cross the epithelium. The possibility that, in the intestine, fructose can form a stable, soluble chelate with magnesium has been demonstrated under *in vitro* conditions by Charley *et al.* [24].

Although the high fructose diet contained slightly less calcium and slightly more phosphorus than the starch diet, it is unlikely that the small change in the Ca/P ratio contributed to a lower calcium balance. Spencer *et al.* [25] demonstrated that high phosphorus intakes did not interfere with calcium absorption over a ten-fold range of calcium intakes. This supported the view of some investigators [26,27] and the World Health Organization [28] that the dietary Ca/P ratio in humans does not play an important role in terms of the utilization and retention of calcium. However, in these studies, a decrease in urinary calcium was reported with increased phosphorus intake [20]. In this study, urinary losses of calcium as a percent of calcium intake were significantly ($p < 0.01$) higher during the high fructose intake (and higher phosphorus intake) periods than during the starch dietary periods.

The increased urinary excretion of phosphorus and negative phosphorus balance when high dietary fructose was fed are consistent with studies of Bergstra *et al.* [29], who found that dietary fructose induced greater urinary concentrations of phosphorus and lowered urinary pH in female rats when compared with glucose. They suggested that the increased urinary excretion of phosphorus was the result of increased absorption from the diet. In this study there was an apparent increase in the absorption of phosphorus from the diet (100 percent of dietary phosphorus in feces). However, more phosphorus was lost in the urine than could be accounted for by both increased dietary intake and increased absorption.

Although plasma phosphate and PTH were unaffected by dietary treatment in this study, the large negative phosphorus balance during the high fructose, low magnesium dietary period may be of some concern. It is likely that longer periods of negative phosphorus balance could lead to a phosphate deficiency and hypophosphatemia. Hypophosphatemia has been observed in patients receiving parenteral nutrition or after infusions of fructose [30]. It was suggested that the hypophosphatemia found after fructose administration was the result of unregulated uptake of fructose by the liver and consequent formation of fructose-1-phosphate [31] and increased phosphate turnover. Some long-term consequences of hypophosphatemia include muscular weakness, cardiomyopathy, bone pain and osteomalacia or rickets [30,32].

The lower retention of calcium and greater losses of phosphorus when large amounts of fructose were fed, particularly in combination with a magnesium low diet, suggests an adverse impact on bone health if the trend continued over a longer period of time. This is consistent with findings of Nguyen *et al.* [33], who found increased urinary calcium losses after fructose infusion, and those of Guthmann *et al.* [34], who demonstrated a stimulation of bone calcium release by carbohydrate. These observations may be of concern from a public health standpoint since the intake of magnesium has decreased appreciably since the beginning of this century [9,10], while fructose consumption has been increasing rapidly since the introduction of high fructose corn syrup in 1970 [1]. This trend seems to be the most

dramatic in children in the US, who are consuming large amounts of soft drinks containing high fructose corn syrup [35] at the expense of foods containing adequate amounts of magnesium and calcium. Thus, additional studies are indicated to determine if a high fructose containing diet combined with low dietary magnesium and marginal calcium leads to bone loss.

ACKNOWLEDGMENTS

We thank the members of the Grand Forks Human Nutrition Research Center clinical staff whose special talents and skills made this study possible: LM Klevay (medical supervision), HC Lukaski (exercise physiology), B Vetter (nursing care), B Hoverson and staff (dietary), L Johnson (statistical analysis), and S Gallagher and the Analytical Biochemistry Laboratory staff (clinical chemistry).

REFERENCES

1. Park KY, Yetley EA: Intakes and food sources of fructose in the United States. *Am J Clin Nutr* 58(Suppl.):737S–747S, 1993.
2. Reiser S, Powell AS, Scholfield DJ, Panda P, Ellwood KC, Canary JJ: Blood lipids, lipoproteins, apoproteins, and uric acid in men fed diets containing fructose or high-amylose cornstarch. *Am J Clin Nutr* 49:832–839, 1989.
3. Swanson JE, Laine DC, Thomas W, Bantle JP: Metabolic effects of dietary fructose in healthy subjects. *Am J Clin Nutr* 55:851–856, 1992.
4. Fields M, Ferretti RJ, Reiser S, Smith JC Jr: The severity of copper deficiency in rats is determined by the type of dietary carbohydrate. *Proc Soc Exp Biol Med* 175:530–537, 1987.
5. Koh ET, Reiser S, Fields M: Dietary fructose as compared to glucose and starch increases the calcium content of kidney of magnesium-deficient rats. *J Nutr* 119:1173–1178, 1989.
6. Gershoff SN, Andrus SB: Effect of vitamin B₆ and magnesium on renal deposition of calcium oxalate reduced by ethylene glycol administration. *Proc Soc Exp Biol Med* 109:99–102, 1963.
7. Heaton FW, Anderson CK: The mechanism of renal calcification induced by magnesium deficiency in the rat. *Clin Sci* 28:99–106, 1975.
8. Koh ET, Min KW: Dietary fructose produces greater nephrocalcinosis in female than in male magnesium-deficient rats. *Magnesium Res* 4:97–103, 1991.
9. U.S. Agricultural Research Service: "Food and Nutrient Intake of Individuals in the United States, Spring 1965. USDA Household Food Consumption Survey, 1965–66." Washington, DC: Consumer and Food Economics Research Division, USDA, 1975.
10. Science and Education Administration: "Food and Nutrient Intakes of Individuals in One Day in the United States, Spring 1977. Nationwide Food Consumption Survey, 1977–78. Preliminary Report 2." Washington, DC: USDA, 1980.
11. Harris JA, Benedict FG: "A Biometric Study of Basal Metabolism in Men." Carnegie Pub No 279. Philadelphia: JB Lippencott Co, 1919.
12. Sims RL, Mullen LM, Milne DB: Application of inductively coupled plasma emission spectroscopy to multielement analysis of foodstuffs used in metabolic studies. *J Food Comp Anal* 3:27–37, 1990.
13. Analytical Methods Committee: Methods of destruction of organic matter. *Analyst* 85:642–656, 1960.
14. Bowers GN Jr, Rains TC: Measurement of total calcium in biological fluids: flame atomic absorption spectrometry. *Methods Enzymol* 158:302–319, 1988.
15. D'Costa M, Cheng P: Ultrafilterable calcium and magnesium in ultrafiltrates of serum prepared with the Amicon MPS-1 system. *Clin Chem* 29:519–522, 1983.
16. Daly JS, Ertingshausen G: Direct method for determining inorganic phosphate in serum with the "CentrifChem." *Clin Chem* 18:263–265, 1972.
17. Kleinbaum DG, Kupper LL: "Applied Regression Analysis and Other Multivariable Methods." North Scituate, MA: Duxbury Press, pp 351–88, 1978.
18. Food and Nutrition Board: "Recommended Dietary Allowances," 10th ed. Washington, DC: National Academy Press, pp 187–94, 1989.
19. Holbrook JT, Smith JC Jr, Reiser S: Dietary fructose or starch: effects on copper, zinc, iron, manganese, calcium, and magnesium balances in humans. *Am J Clin Nutr* 49:1290–1294, 1989.
20. Hallfrisch J, Powell A, Carafelli C, Reiser S, Prather ES: Mineral balances of men and women consuming high fiber diets with complex or simple carbohydrate. *J Nutr* 117:48–55, 1987.
21. Ivaturi R, Kies C: Mineral balances in humans as affected by fructose, high fructose corn syrup and sucrose. *Plant Foods for Hum Nutr* 42:143–151, 1992.
22. Hallfrisch J: Metabolic effects of dietary fructose. *FASEB J* 4:2652–2660, 1990.
23. Van der Heijden A, Van den Berg GJ, Lemmens AG, Beynen AC: Dietary fructose v. glucose in rats raises urinary excretion, true absorption and ileal solubility of magnesium but decreases magnesium retention. *Brit J Nutr* 72:567–577, 1994.
24. Charley PJ, Sarkar B, Stitt CF, Saltman P: Chelation of iron by sugars. *Biochem Biophys Acta* 69:313–321, 1963.
25. Spencer H, Kramer L, Osis D, Norris C: Effect of phosphorous on the absorption of calcium and on the calcium balance in man. *J Nutr* 108:447–457, 1978.
26. Hegsted DM: Mineral intake and bone loss. *Fed Proc* 26:1747–1754, 1967.
27. Spencer H, Kramer L, Osis D: Factors contributing to calcium loss in aging. *Am J Clin Nutr* 36:776–787, 1982.
28. "World Health Organization Technical Report Series, No. 230. Calcium Requirements." Geneva: WHO, pp 16–18, 1962.
29. Bergstra AE, Lemmens AG, Beynen AC: Dietary fructose vs glucose stimulates nephrocalcinogenesis in female rats. *J Nutr* 123:1320–1327, 1993.
30. Crook M, Swaminathan R: Disorders of plasma phosphate and indications for its measurement. *Ann Clin Biochem* 33:376–396, 1996.
31. Knochel JP, Agarwal R: Hypophosphatemia and hyperphos-

- phatemia. In Brenner BM, (ed: "The Kidney," 5th ed. Philadelphia, PA: WB Saunders, pp 1086–1133, 1996.
32. Stoff JS: Phosphate homeostasis and hypophosphatemia. *Am J Med* 72:489–495, 1982.
33. Nguyen NU, Dumoulin G, Henriet MT, Regnard J: Increase in urinary calcium and oxalate after fructose infusion. *Horm Metab Res* 27:155–158, 1995.
34. Guthmann HM, Palmieri GMA, Hinton AB, Guthmann AL: The mechanism of insulin-induced hypercalcemia in the chick. *Endocrinology* 110:571–574, 1982.
35. Nicklas TA, Myers L, Beech B, Berenson GS. Trends in dietary intake of sugars of 10-year-old children from 1973 to 1988: the Bogalusa heart study. *Nutr Res* 19:519–530, 1999.

Received September 1999; revision accepted November 1999.